IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PAR PHARMACEUTICAL, INC. and ENDO PAR INNOVATION COMPANY, LLC Plaintiffs, v. ZYDUS PHARMACEUTICALS (USA) INC. and ZYDUS LIFESCIENCES LTD. Defendants.	Civil Action No. _____

COMPLAINT

This is a complaint for patent infringement requesting preliminary and permanent injunctive relief to prevent infringement of U.S. Patent No. 11,717,524 (the "'524 patent"), which claims novel methods for making purified varenicline, a smoking cessation drug. The PTO issued the '524 patent earlier today to plaintiff Par Pharmaceutical, Inc., and it is exclusively licensed to Epic Par Innovation Company, LLC (collectively "Par"). In a race to the market, the Defendants Zydus Pharmaceuticals (USA) Inc. and its parent corporation Zydus Lifesciences Ltd. (collectively "Zydus") launched their infringing product after Par notified them of the notice of allowance on the '524 patent but before Par could bring suit on the issued patent. Now that the PTO has issued the '524 patent, Par seeks to return the parties to the status quo and for a judgment on the merits that Zydus has infringed and will continue to infringe the patent through the sale of its varenicline tablets. In support thereof, Par alleges as follows:

PARTIES

1. Plaintiff Par Pharmaceutical, Inc. ("Par Pharmaceutical") is a corporation organized and existing under the laws of the State of New York, having a principal place of business at 300 Tice Blvd, Suite 230, Woodcliff Lake, New Jersey 07677. Par Pharmaceutical develops, manufactures, and markets pharmaceutical products in the United States, including in this judicial district.

2. Plaintiff Endo Par Innovation Company ("EPIC") is a limited liability company organized and existing under the laws of Delaware, having its principal place of business at 300 Tice Blvd, Suite 230, Woodcliff Lake, New Jersey 07677.

3. Upon information and belief, defendant Zydus USA is a corporation organized and existing under the laws of New Jersey, having its corporate offices and principal place of business at 73 Route 31 N., Pennington, New Jersey 08534. Zydus USA markets, distributes, sells, and imports generic versions of branded pharmaceutical products developed and/or manufactured by Zydus Lifesciences throughout the United States, including in this judicial district.

4. Upon information and belief, defendant Zydus Lifesciences is a corporation organized and existing under the laws of India, having its corporate offices and principal place of business at Zydus Corporate Park, Scheme No. 63, Survey No. 536, Khoraj (Gandhinagar), Nr. Vaishnodevi Circle, S.G. Highway, Ahmedabad 382481, Gujarat, India. Zydus Lifesciences, either directly or through Zydus USA and/or its other agents, markets, distributes, sells, and/or imports generic versions of branded pharmaceutical products throughout the United States, including in this judicial district.

NATURE OF ACTION

5. This is an action for infringement of United States Patent No. 11,717,524 ("the '524 patent"). This action is based upon the Patent Laws of the United States, 35 U.S.C. § 100, *et seq*. A copy of the '524 patent is attached hereto as Ex. 1.

JURISDICTION AND VENUE

6. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a) (patent infringement).

7. This Court has personal jurisdiction over Zydus USA and Zydus Lifesciences.

8. Zydus USA and Zydus Lifesciences are agents of each other and acting in concert with each other with respect to the manufacturing and importing into the United States the generic varenicline tablets, in 0.5 and 1 mg dosage strengths (as detailed below), that Par accuses of infringement in this matter, as well as the distribution and sale of those products throughout the United States and in this judicial district.

9. This Court has personal jurisdiction over Zydus USA because, *inter alia*, it has purposefully availed itself of the privilege of doing business in Delaware directly or indirectly through its subsidiaries or agents; maintains pervasive, continuous, and systematic contacts with the State of Delaware, including through the marketing, distribution, and sale of its generic versions of branded pharmaceutical products in the State of Delaware; derives substantial revenue from the importation and sale of its products in the State of Delaware; and manufactures the products accused of infringement in this case, including those that are marketed, distributed, and sold in the State of Delaware.

10. This Court has personal jurisdiction over Zydus Lifesciences because, *inter alia*, Zydus Lifesciences has purposefully availed itself of the privilege of doing business in Delaware

directly or indirectly through its Zydus USA and/or other subsidiaries or agents; maintains pervasive, continuous, and systematic contacts with the State of Delaware, including through the marketing, distribution, and sale of its generic versions of branded pharmaceutical products in the State of Delaware; derives substantial revenue from the importation and sale of its products in the State of Delaware; and manufactures the products accused of infringement in this case, including those that are marketed, distributed, and sold in the State of Delaware.

11. In the alternative, this Court may also exercise jurisdiction over Zydus Lifesciences pursuant to Fed. R. Civ. P. 4(k)(2) to the extent that Zydus Lifesciences, as a foreign defendant, is not subject to personal jurisdiction in any state's court of general jurisdiction, based on Zydus Lifesciences' contacts with the United States as a whole, including without limitation through the importation, distribution, and sales of its pharmaceutical products throughout the United States, including in this district.

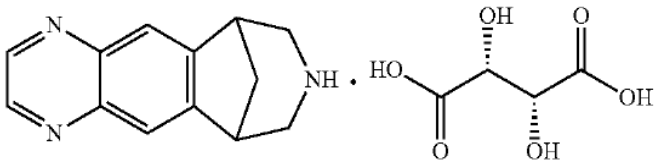
12. Venue as to Zydus USA is proper in this district pursuant to 28 U.S.C. §§ 1391 and 1400(b) because, *inter alia*, Zydus USA is subject to personal jurisdiction in this district, has previously consented to venue in this judicial district, and on information and belief has committed acts of infringement in this judicial district and is subject to venue in this judicial district for purpose of this case. Zydus USA has consented to venue in this judicial district in other patent litigations, including but not limited to the following actions: *Acadia Pharmaceuticals Inc. v. Zydus Pharmaceuticals (USA) Inc. et al.*, C.A. No. 22-cv-01386-GBW (D. Del.); *Novo Nordisk Inc., et al. v Zydus Worldwide DMCC, et al.*, C.A. No. 22-297-CFC (D. Del.); *Astrazeneca AB, et al. v. Zydus Pharmaceuticals (USA) Inc., et al*., C.A. No. 21-550-RGA (D. Del.).

13. Venue as to Zydus Lifesciences is proper in this district pursuant to 28 U.S.C. §§ 1391(c), and 1400(b) because, *inter alia*, Zydus Lifesciences is a foreign corporation and as such may be sued in any judicial district in the United States in which Zydus Lifesciences is subject to the court's personal jurisdiction.

FACTUAL BACKGROUND

Nitrosamine Impurities in Varenicline Tartrate Products

14. Varenicline tartrate is a synthetic drug useful in treating nicotine dependency, addiction, and withdrawal. It has the following chemical formula:

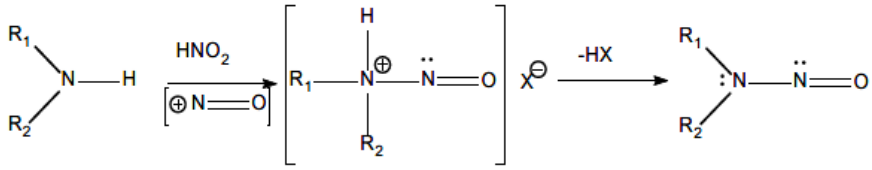


15. In 2006, the FDA authorized Pfizer to make and sell varenicline tartrate tablets under the trade name CHANTIX® as a partial agonist selective for certain subtypes of nicotinic receptors and indicated for smoking cessation. At its height, Pfizer's revenues from its sales of CHANTIX® were in excess of $1 billion per year.

16. However, due to the presence of unacceptably high levels of a nitrosamine impurity (N-nitroso-varenicline) associated with potential increased cancer risk in humans, Pfizer withdrew CHANTIX® from the market in or about July 2021.

17. As described in FDA guidance concerning the control of nitrosamine impurities in pharmaceutical drug products, nitrosamines are a class of compounds with a chemical structure in which a nitroso group is bonded to an amine (R1N(-R2)-N=O), which can form by a nitrosating reaction between amines and nitrous acid, as shown in the following figure:

Figure 1. Representative Reaction to Form Nitrosamines



See Ex. 2 ("Control of Nitrosamine Impurities in Human Drugs", Guidance for Industry, U.S. Food and Drug Administration Center for Drug Evaluation and Research (Feb. 2021, Rev. 1)), at 3-4 and Figure 1.

18. The unexpected discovery in 2018 and 2019 of the presence of nitrosamines in several pharmaceutical drug products led the FDA and other international regulators to conduct a detailed analysis of these impurities in affected active pharmaceutical ingredients ("API") and drug products and the potential root causes of their presence in those products. Based on that analysis, in September 2020, the FDA issued guidance to pharmaceutical manufacturers, including recommendations for evaluating the risk for nitrosamine contamination or formation in their APIs and drug products and the establishment of acceptable daily intake limits for particular nitrosamine impurities found in drug products. The FDA updated that guidance in February 2021. *See* Ex. 2.

19. In connection with that evaluation and guidance, in September 2020, the FDA established an acceptable daily intake limit (AI) of varenicline nitrosamine impurities of 37 nanograms, which equates to 18.5 parts per million ("ppm") of those impurities per 1 mg of varenicline API for CHANTIX® and other FDA-approved varenicline tartrate smoking cessation products.

20. On July 2, 2021, the FDA announced that Pfizer had discovered the presence of N-nitroso-varenicline at levels above FDA's acceptable intake limit in nine commercial lots of CHANTIX® and that, as a result, Pfizer was recalling those lots from warehouses. Pfizer

subsequently expanded that recall and discontinued sales of CHANTIX®. *See, e.g.,* https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-nitrosamine-varenicline-chantix; Fed. Reg., Vol. 88, No. 38 at 12384-85.

21. Despite how successful sales of CHANTIX® were, Pfizer has been unable in the two years since it pulled CHANTIX® from the market to reformulate its varenicline tartrate tablets so as to reduce the nitrosamine impurities in them to a level that meets the FDA-mandated acceptable daily intake limits. Accordingly, Pfizer no longer sells any varenicline tartrate products.

22. In February 2023, the FDA announced that it would not approve any future abbreviated new drug applications ("ANDAs") for varenicline tartrate drug products that do not meet the applicable acceptable daily intake limits for nitrosamine impurities. *See* Fed. Reg., Vol. 88, No. 38 at 12384-85.

Par's Varenicline Tartrate Products

23. Par Sterile was a first filer of an ANDA (ANDA No. 2011785) for varenicline tartrate products, seeking FDA approval to generic varenicline tartrate tablets in 0.5 mg and 1 mg dosage strengths.

24. When Par scientists began working on Par's varenicline tartrate tablets, there was no published literature about the presence of nitrosamine impurities in varenicline products, let alone public information about the specific chemical structure of any such impurities or about how to detect them. Accordingly, the Par scientists were effectively starting from scratch in terms of seeking to identify and control the extent of varenicline-related nitrosamine impurities that might be found in Par's varenicline API.

25. Par engaged in extensive work to develop analytical methods to identify, detect, and quantify the nitrosamine impurities in its varenicline API, as well as a commercially practicable method for reducing those impurities to acceptable levels.

26. In contrast to Pfizer's CHANTIX® products, Par successfully developed varenicline tablets that have remarkably low levels of nitrosamine impurities—less than 5 ppm per 1 mg of varenicline API, *i.e.*, well below the FDA's acceptable daily intake limit of 18.5 ppm.

27. Accordingly, on August 11, 2021, the FDA approved Par's ANDA. Upon information and belief, Par was the only ANDA filer that, at the time, had been able to develop varenicline tartrate tablets with nitrosamine levels that satisfied the FDA's acceptable intake limit for nitrosamine impurities.

28. Indeed, in February 2022, the FDA posted the results of testing it had conducted on several other varenicline tartrate tablets, and those results showed that Par's varenicline tablets have dramatically lower nitrosamine levels than any of the other commercially available products:

Company (Manufacturer)	Product	Lots Tested	N-nitroso-varenicline level in micrograms/tablet (nanograms/tablet)	N-nitroso-varenicline level in parts per million (ppm)
Pfizer	Chantix (varenicline) 1mg	EA6080, EC9841, EC9847, EC9848, EX2099, DR5086	0.15-0.47 (150-470)	155-474
Par Pharmaceuticals	Varenicline 1 mg	31960807, 31960801	0.003 (3)	3
Apotex	APO-Varenicline Tartrate 1 mg)	TG2183, TG2181, TG2182	0.027-0.044 (27-44)	27-44
Apotex	APO-Varenicline Tartrate 0.5 mg	TG2180, TG2178, TG2179	0.014-0.021 (14-21)	27-42

See Ex. 3 ("Laboratory analysis of varenicline products", FDA Feb. 8, 2022).

29. Because the nitrosamine levels in those other tablets exceeded the FDA's acceptable daily intake levels, each of them had to be withdrawn from the market. The FDA granted Apotex Corp. a limited waiver to sell varenicline tablets to ensure adequate supply to the U.S. market, but that waiver expired as of at least May 2022.

30. Making varenicline tartrate tablets with the low levels of nitrosamine required by the FDA is difficult to do, as evidenced by the fact that Pfizer has been unable to reformulate its CHANTIX® product to meet those requirements despite the huge incentive it has had to do so (*i.e.*, the loss of a product that had $1 billion in annual revenues).

Par's Patented Technology

31. As the first, and at the time only, pharmaceutical manufacturer able to overcome the difficulties associated with developing FDA-approvable varenicline tartrate tablets with nitrosamine impurities below the FDA's acceptable daily intake level—which other

manufacturers like Pfizer have been unable to do, Par filed patent applications directed to its novel technologies for manufacturing varenicline tartrate tablets with low levels of nitrosamine impurities, including U.S. Patent Application No. 17/930,824 (the "'824 application").

32. On June 7, 2023, the United States Patent and Trademark Office ("PTO") issued a Notice of Allowance and Fee(s) Due, stating that the then-pending patent claims of the '824 application would be allowed for patenting.

33. Thereafter, on August 8, 2023, the PTO issued the '524 patent, titled "Varenicline Compound and Process of Manufacture Thereof." Representative claim 1 of the '524 patent recites the following:

> 1. A method of making a varenicline tartrate tablet comprising less than 50 ppm of nitrosamine impurities, the method comprising:
> (a) mixing varenicline free base with tartaric acid to form varenicline tartrate
> (b) means for reducing the nitrosamine impurities to less than 50 ppm per tablet as measured by LC-ESI-HRMS Method;
> wherein the means comprises an acid-base treatment.

Ex. 1, claim 1.

34. Earlier, on March 14, 2023, the PTO had issued to Par U.S. Patent No. 11,602,537 (the "'537 patent"). The claims of the '537 patent are directed to Par's novel pharmaceutical varenicline tartrate tablet compositions.

35. Par Pharmaceuticals is the assignee and owner of the '524 patent, and EPIC is an exclusive licensee of that patent.

Zydus's Infringement of the '524 Patent

36. Upon information and belief, Zydus USA submitted an ANDA (ANDA No. 216723, the "Zydus ANDA") pursuant to 35 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture and sale of generic varenicline tartrate tablets in the same 0.5 mg and 1 mg dosage strengths as sold by Par (the "Accused Tablets").

37. Par became aware of the Zydus ANDA, and therefore, on May 17, 2023, Par wrote Zydus a notice letter advising Zydus of Par's patented technologies, including those embodied in Par's '537 patent, which had just been granted, and in Par's pending patent applications (which included the '824 application) ("First Notice Letter"). A copy of the First Notice Letter is attached as Ex. 4.

38. Then, on June 9, 2023, Par wrote Zydus a second notice letter, advising Zydus that the PTO had just issued the Notice of Allowance with respect to the '824 application ("Second Notice Letter"). A copy of the Second Notice Letter is attached as Ex. 5.

39. Among other things, the Second Notice Letter notified Zydus of the scope of a representative allowed claim of the '824 application (which issued as claim 1 of the '524 patent, recited above); advised Zydus that Par believed it was highly likely that Zydus's proposed varenicline tartrate tablets, if approved by the FDA, would infringe that claim; and requested that Zydus notify Par if it believed that those tablets would not infringe Par's patent rights, including the basis for any such belief.

40. The Second Notice Letter further advised Zydus that if Par sued to enforce the allowed claims of the '824 application, once issued, Zydus would have the burden, pursuant to 35 U.S.C. § 295, of establishing that its tablets are not made in accordance with Par's patented manufacturing process.

41. Thereafter, on June 12, 2023, the FDA approved the Zydus ANDA. The following day, Zydus issued a press release announcing the approval and stating that Zydus would launch its tablets "shortly." A copy of that press release is attached as Ex. 6.

42. The approved prescribing information and labeling for the Accused Tablets states that they will be manufactured by Zydus Lifesciences in India and distributed in the United

States by Zydus USA. A copy of the approved prescribing information and labeling is attached as Ex. 7.

43. Zydus did not respond to the First or Second Notice Letters until June 21, 2023. On that date, James Peterka from the Locke Lord law firm emailed counsel for Par advising that he was representing Zydus in connection with those Notice Letters and would respond further to them "in due course." A copy of that email is attached as Ex. 8.

44. Later that day, Par's counsel sent Mr. Peterka a third notice letter reiterating its belief that Zydus's newly-approved varenicline tartrate tablets would infringe the allowed claims of the '824 application, which the PTO would soon be issuing as a granted U.S. patent, and further describing the basis for Par's belief in that regard ("Third Notice Letter"). A copy of the Third Notice Letter is attached as Ex. 9.

45. In particular, the Third Notice Letter advised that Par believed it was highly likely that the Accused Tablets would infringe the allowed claims of the '824 application (now the '524 patent) because:

- The approved label confirms that the API in the Accused Tablets is varenicline tartrate, as claimed: "Varenicline tablets contain varenicline (as the tartrate salt), which is a partial nicotinic agonist selective for α β nicotinic acetylcholine receptor subtypes." Ex. 7 (FDA-approved prescribing information and label for the Accused Tablets) at 17.
- We know that the Accused Tablets will contain less than 50 ppm of nitrosamine impurities, as claimed, because the FDA's acceptable intake limit for the claimed nitrosamine impurities is only 37 ng per day, which translates to 18.5 ppm. *See, e.g.,* https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-nitrosamine-varenicline-chantix.
- The only commercially-viable methods for making varenicline tartrate tablets with the claimed low levels of nitrosamine impurities that Par is aware of are the methods taught and claimed in the '824 application, such that Par believes it is highly likely that Zydus is using those methods (or an equivalent thereof) to make the Accused Tablets.

See Ex. 9 (Third Notice Letter).

46. The Third Notice Letter also repeated Par's request that Zydus identify the basis for any belief that it is not utilizing Par's patented manufacturing methods and reiterated that in any lawsuit enforcing Par's patent rights, Zydus would have the burden of establishing that it is not using those methods to make the Accused Tablets.

47. Zydus has not responded to the Third Notice Letter, nor has it provided the promised further response to the First and Second Notice Letters.

48. Since receiving the Third Notice Letter, Zydus launched the Accused Tablets and has been marketing and selling them in the United States with willful disregard for Par's patent rights.

49. Par has been unable to ascertain the processes that Zydus uses to manufacture its varenicline API and the Accused Tablets, or have them made, despite having made diligent and reasonable efforts to do so. In particular and among other things:

A. Upon information and belief, detailed information about those manufacturing processes is contained in the Zydus ANDA and/or the accompanying Drug Master File ("DMF") for the varenicline API contained in the Accused Tablets, both of which would have been submitted to the FDA and are maintained by the FDA on a confidential basis. The FDA publishes a list of DMFs filed with the agency. That list identifies 17 DMFs for varenicline tartrate, and Zydus is not identified as the holder of any of those DMFs. Par has not been able to determine which DMF relates to the varenicline API used in Zydus's tablets, and even if it could, Par would not be able to obtain a copy of the relevant portions of the DMF from the FDA. Likewise, Par is unable to obtain the relevant portions of the Zydus ANDA from the FDA.

B. Par has written to Zydus on multiple occasions to try to ascertain any basis on which Zydus might claim that it is not using Par's patented technologies and has asked Zydus to provide information about its manufacturing processes, including the relevant portions of its ANDA and the DMF, to Par's outside counsel on a confidential basis subject to a non-disclosure agreement. *See* Ex. 9 (Third Notice Letter, with enclosure). That is similar to the process used in most Hatch-Waxman Act patent litigation proceedings in which the generic manufacturer makes an Offers of Confidential Access to its ANDA pursuant to 21 U.S.C. § 355(c)(3)(D)(i)(III) and 21 C.F.R. § 314.52(c)(7) ("OCAs") so as to provide the patent holder with the information necessary to evaluate possible claims of patent infringement and decide whether to bring suit under the Act. Indeed, Zydus undoubtedly has served numerous OCAs in connection with other generic products. However, Zydus refused to provide any information to Par or its outside counsel about the manufacturing processes used to make the Accused Tablets or the varenicline API used therein.

COUNT I
INFRINGEMENT OF THE '524 PATENT

50. Par incorporates each of the preceding paragraphs as if fully set forth herein.

51. Upon information and belief, Zydus's manufacture, importation, and commercial sale of the Accused Tablets constitutes infringement of the '524 patent under at least 35 U.S.C. § 271(b) and (g), including without limitation claim 1 thereof as recited above.

52. In particular, for the reasons described in the Third Notice Letter, among others, Par believes that it is highly likely that Zydus is making the varenicline API used in the Accused Tablets, or having it made, in accordance with the manufacturing methods taught and claimed in the '524 patent, and that Zydus is thereafter importing them into the United States and selling them throughout the United States.

53. Par has used its best efforts to confirm its beliefs in that regard, including the following:

A. As noted above, the approved prescribing information and labeling confirms that the API in the Accused Tablets is varenicline tartrate, as claimed: "Varenicline tablets contain varenicline (as the tartrate salt), which is a partial nicotinic agonist selective for α β nicotinic acetylcholine receptor subtypes." Ex. 7 (FDA-approved prescribing information and label for the Accused Tablets) at 17.

B. Par obtained samples of the Accused Tablets and had them tested by an independent third-party laboratory (Averica) to determine the levels of nitrosamine impurities in the Tablets. Their testing showed that each of the sample Accused Tablets tested had nitrosamine levels below 2 ppm, *i.e.*, within the ranges claimed in the '524 patent.

C. Par has been unable to ascertain the processes that Zydus uses to manufacture its varenicline API and the Accused Tablets, or have them made, despite having made diligent and reasonable efforts to do so, as summarized above.

54. In light of the above, upon information and belief, Par believes it is highly likely that Zydus is making the Accused Tablets via the manufacturing methods taught and claimed in the '524 patent, including without limitation claim 1 thereof.

55. Upon information and belief, Zydus is manufacturing the Accused Tablets in India and importing them in the United States for commercial sale throughout the country.

56. With full knowledge of the '524 patent and willful disregard of Par's accompanying patent rights, Zydus has continued and is continuing to make, import, and sell the Accused Products following issuance of the '524 patent, thereby infringing the '524 patent under at least 35 U.S.C. § 271(b) and (g).

57. Zydus's infringement has caused and is continuing to cause Par to suffer significant damage. If unchecked, Zydus's ongoing infringement will continue to inflict additional significant and irreparable harm upon Par.

58. Zydus's infringement of the '524 Patent is willful.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

A. A judgment that Zydus has infringed the '524 Patent;

B. Preliminary and permanent injunctive relief restraining and enjoining Zydus, its officers, agents, servants and employees, and those persons in active concert or participation with any of them, from infringement of the '524 patent for the full term thereof, including any extensions;

C. An award of monetary damages, including pre and post-judgment interest;

D. A finding that Zydus's infringement has been willful and an award of enhanced damages trebling any monetary relief awarded to Plaintiffs;

E. Reasonable attorneys' fees, filing fees, and reasonable costs of suit incurred by Plaintiffs in this action; and

F. Such other and further relief as the Court may deem proper and just.

Dated: August 8, 2023

Respectfully submitted,

FARNAN LLP

/s/ Michael J. Farnan

Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 North Market St.
12th Floor
Wilmington, DE 19801
Tel: 302-777-0300
Fax: 320-777-0301
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

Attorneys for Plaintiffs Par Pharmaceutical, Inc. and Endo Par Innovation Company, LLC

OF COUNSEL:

Martin J. Black
Robert D. Rhoad
Sharon K. Gagliardi
Brian M. Goldberg
Luke M. Reilly
Daniel R. Roberts
DECHERT LLP
Cira Centre
2929 Arch Street
Philadelphia, PA 19104
Tel: (215) 994-4000
martin.black@dechert.com
robert.rhoad@dechert.com
sharon.gagliardi@dechert.com
brian.goldberg@dechert.com
luke.reilly@dechert.com
daniel.roberts@dechert.com

Jonathan D.J. Loeb, Ph.D.
DECHERT LLP
2400 W. El Camino Real, Suite 700
Mountain View, CA 94040-1499
Tel: (650) 813-4995
jonathan.loeb@dechert.com